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CELL THERAPY

310 T cell therapy with EBV-specific cytotoxic T-lymphocytes for patients with nasopharyngeal carcinoma

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Background: Nasopharyngeal carcinoma (NPC) is an Epstein-Barr virus (EBV)-related, highly chemo-radiosensitive malignancy. However, one-third of patients are considered to be incurable because of metastatic or recurrence disease. Expression of antigenic viral proteins by malignant cells constitutes a good target for immunotherapeutic strategies. Although the majority of clinical data have been obtained in the setting of EBV-related posttransplant lymphoproliferative disorders, this therapeutic approach has been more recently applied to solid tumors.

Methods: We and others have implemented T-cell therapy programs for patients with NPC failing conventional treatment. The feasibility of expanding EBV-targeted cytotoxic T lymphocytes (CTL) by stimulation with EBV-transformed lymphoblastoid cell lines (LCLs) has been demonstrated, and clinical trials were conducted, based on administration of 2 or more doses of EBV-CTLs (4-40 x 10^7/dose), supported by in vivo rhIL-2 infusion and, in some cases, pre-treatment with lymphodepleting chemo or immunotherapy.

Results: So far, more than 60 patients were treated in different centers for refractory/relapsed advanced NPC, and about 20% objective responses, including some complete responses, were observed, with no or limited adverse events. These results are encouraging, although further improvements to the laboratory and clinical protocols are clearly necessary to increase anti-cancer activity. One approach that our center has lately pursued is to test the efficacy of CTL therapy in earlier stages of disease, in particular immediately after first line chemotherapy for relapsed disease. The clinical results of this attempt seem to improve overall survival as compared with conventional therapies, and justify a prospective trial in this specific setting.

Conclusions: EBV-specific CTL therapy is safe and associated with clinical benefit in patients with refractory or metastatic NPC. Sequential combination of CTL therapy with other agents, such as checkpoint inhibitors, could yield optimal results.

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